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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,659	07/20/2000	Tommy Abrahamsson	1103326 0629	9094

7590

12/10/2002

White & Case  
Patent Department  
1155 Avenue of the Americas  
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EXAMINER

LUKTON, DAVID

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 12/10/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/600,659

Applicant(s)

ABRAHAMSSON ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-23,25-33 and 41-63 is/are pending in the application.
- 4a) Of the above claim(s) 3,9-23,25-33 and 43-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-8, 41, 42 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

Pursuant to preliminary amendment, claims 24, 34-40 have been cancelled, claims 1-3, 8-11, 15-19, 23, 25, 27, 28, 30, 32, 33 amended, and claims 41-63 added.

Claims 1-23, 25-33, 41-63 remain pending.

Applicants election of Group 1 without traverse (claims 1, 2, 4-8, 41, 42, limited to G1) is acknowledged, as are the elected species ("compound A" and melagatran).

The abbreviation "CPU" hereinbelow refers to carboxypeptidase U.

\*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-8, 41, 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is asserted (page 33, line 1+) that the following diseases can be successfully treated with the combination of the CPU and thrombin inhibitor: Lupus anticoagulant, homocysteinemia, thrombocytopenia, Alzheimer's disease, venous thrombosis, pulmonary embolism, arterial thrombosis, systemic embolism, disseminated intravascular coagulation, restenosis,

respiratory distress syndrome, pulmonary fibrosis, septicemia, edema, atherosclerosis, coronary arterial disease, and cerebral arterial disease. However, applicants have not shown that any of these diseases can be successfully treated using the claimed compositions. It may be the case that there exist a small number of thrombin inhibitors which have exhibited efficacy in the treatment of one or more of these diseases, but it does not follow therefrom that all thrombin inhibitors, regardless of anti-thrombic potency, will also be effective. It is suggested that the term "pharmaceutical" be deleted from the claims.

✱

Claim 2 is rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 2, it is recited that variable R2 can be oxo. However, this is not the case. No matter what R3 is, it is impossible for R2 to be oxo. In traversing this ground of rejection, applicants are requested to provide an example of a structure in which R2 is oxo, and at the same time, R3 is one of the recited substituents.

✱

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention

was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Ondetti (USP 4,177,277) in view of Grainger (USP 6,410,587) or Watson (USP 6,326,386) or Franson (USP 6,020,510).

Ondetti discloses (col 3, line 18+) compounds that are inhibitors of carboxypeptidase U and as such are useful in the treatment of inflammation. Ondetti does not suggest combining these compounds with thrombin inhibitors. Each of the secondary references teaches that thrombin inhibitors can be used to treat inflammation, or else that compounds exist which are useful to treat inflammation, and at the same time inhibit thromin. Relevant passages are as follows:

- Grainger discloses (col 22, line 32+) compounds which serve the dual role of thrombin inhibitor and anti-inflammatory agent.
- Franson discloses (col 7, line 58+) compounds that inhibit thrombin-induced platelet aggregation, and at the same time, can be used to treat various inflammatory conditions.

- Watson discloses (col 1, lin 55+) that thrombin inhibitors can be used to treat inflammation

Thus, one of ordinary skill would have been motivated to combine the anti-inflammatory compounds of Ondetti with the anti-inflammatory compounds of the secondary references. The resulting compositions would then contain an inhibitor of CPU as well as an inhibitor of thrombin.

Thus, the claim is rendered obvious.

✱

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Bajzar (USP 5,993,815).

Bajzar discloses inhibitors of carboxypeptidase U. Also disclosed (col 7, line 33+) is that such inhibitors will be useful to treat thrombosis, stroke, and myocardial infarction. Bajzar does not teach that thrombosis, stroke, or myocardial infarction should be treated with a thrombin inhibitor. However, cardiologists of ordinary skill are aware that thrombin inhibitors are useful for this purpose. Thus, a cardiologist of ordinary skill would have been motivated to combine an inhibitor of carboxypeptidase U with a thrombin inhibitor for additive effects.

✱

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Ondetti (USP 4,177,277) in view of Bajzar (*J Biol Chem* 271 16603, 1996) or Boffa (*J Biol Chem* 273

2127, 1998).

Ondetti discloses (col 3, line 18+) compounds that are inhibitors of carboxypeptidase U and as such are useful in the treatment of inflammation. Ondetti does not suggest combining these compounds with thrombin inhibitors. Bajzar and Boffa both teach that CPU is formed by the action of thrombin. Neither Bajzar nor Boffa suggests combining a CPU inhibitor with a thrombin inhibitor. However, given that thrombin is instrumental in the formation of CPU, one of ordinary skill would have been motivated to combine a thrombin inhibitor with a CPU inhibitor to achieve additive effects, i.e., inhibition of the formation of CPU, and inhibition of whatever CPU happens to be formed.

Thus, the claim is rendered obvious.

✱

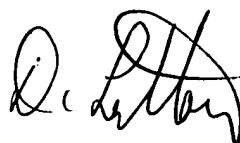
The two applications (09/600660 and 09/600661) were stricken from the IDS. These should be listed under the "other documents" section. Applicants may resubmit an IDS, if deemed appropriate.

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



DAVID LUKTON  
PATENT EXAMINER  
GROUP 1800